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(54) Methanol Extraction of Tocopherol

(57) Tocopherol can be purified by bringing a material containing tocopherol into contact with an amount of methanol that is sufficient to form two phases, one of which is a methanol phase enriched in tocopherol. This methanol phase enriched in tocopherol can then be separated and cooled to an extent that is sufficient to bring about phase formation. This second methanol phase enriched in tocopherol can then be separated and better purified tocopherol can be isolated from it.

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Patent Claims

1. Process for the purification of tocopherol comprised of

(1) bringing a substance containing tocopherol into contact with an amount of methanol that is sufficient to form two phases, these phases consisting of

(A) a methanol phase consisting of tocopherol and some impurities originally contained in the starting material and

(B) a phase of impurities,

(2) separation of the phases,

(3) lowering of the temperature of the substance of phase (A) by an amount that is sufficient for a phase separation to take place and two phases to form, these phases consisting of

(C) a methanol phase enriched in tocopherol and

(D) a raffinate phase of tocopherol and impurities

(4) separation of the phases, and

(5) isolation of tocopherol from the substance of phase (C).

2. Process in accordance with Claim 1, characterized by the fact that step 1 is carried out at a temperature in the range of about 10°C to about 100°C and at a pressure of about 1 to 4 bar (1 to 4 atmospheres) and the temperature of step 3 lies in the range of about -98°C to about 60°C, but with the proviso that the temperature of step 3 be at least about 15°C lower than the temperature of step 1.

3. Process in accordance with Claim 2, characterized by the fact that, after step 2 and before step 3, methanol is removed from the material of phase A.

4. Process in accordance with Claim 1, characterized by the fact that step 1 is carried out at a temperature in the range of about 40°C to about 90°C and at a pressure of about 1 to about 3 bar (about 1 to about 3 atmospheres) and the temperature of step 3 lies in the range of about -10°C to

about 60°C, but with the proviso that the temperature of step 3 be at least about 20°C lower than the temperature of step 1.

5. Process in accordance with Claim 3, characterized by the fact that a continuously operating, multistage countercurrent system is used for the overall process.

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Methanol Extraction of Tocopherol

Tocopherol compounds, also referred to as vitamin E, are the active constituents of certain vegetable oils. The vitamin E activity refers to the physiological activity of this group of foodstuffs. Substances with vitamin E activity all belong to a distinct series of compounds that are all derivatives of chroman-6-ol. These compounds are all tocol derivatives with an isoprenoid C_{16} side chain. The term "tocol" is used to refer to 2-methyl-2-(4',8',12'-trimethyltridecyl)chroman-6-ol. These compounds, called homologues here, are alpha-, beta-, gamma-, and delta-tocopherol, which are of primary importance for vitamin E activity.

Other compounds that likewise show vitamin E activity and are included here in the term "tocopherol" and "tocopherol homologues" are the compounds typically referred to as toco mono-, di-, and trienols. These toco enols differ from the other tocopherol homologues only in that they have an unsaturated isoprenoid C_{16} side chain. Naturally found toco enols are also valuable on account of their vitamin E activity and are typically isolated together with the

saturated tocopherol homologues when these natural sources are exploited for the collection of vitamin E.

These tocopherol homologues are isolated from various natural sources, which are found in widespread natural foodstuffs. They are present in highest concentration in cereal grain oils, particularly in corn and wheat oils, as well as in barley and rye. They are also found in vegetable oils such as safflower, soybeans, peanuts, cottonseed, linseed, sunflower seeds, rapeseed, and palm and in other plant sources.

Naturally occurring tocopherol homologues are generally isolated from natural products, such as vegetable oils as sources, by means of diverse combinations of procedures, such as esterification, saponification, extraction, distillation, ion exchange, adsorption chromatography, precipitation of sterols, and crystallization. The isolated tocopherol concentrate varies depending on the special method of separation employed and, in addition, on the plant source.

A well-known technical activity is the further processing of tocopherols and the quality improvement of non-alpha-tocopherols so as to increase their vitamin E activity. In order to attain this goal, however, it is desirable and even necessary to isolate those tocopherol homologues with vitamin E activity and to separate out the sterols and other impurities.

Included among the known methods of isolation of tocopherols is that described in US-PS 3,402,182, which concerns a process for the separation of mixtures of tocopherol homologues into their individual components by the use of a basic anion-exchange resin. This process tends to be time-consuming and expensive. Furthermore, there exists the risk that the resins will clump together and their activity diminished.

A process of liquid fractionation for the isolation of tocopherols in a purified form from a product stream is described in US-PS 4,454,329. In accordance with this process, one or more organic solvents, including methanol, can be employed in order to come into contact with the esterified hydrogenation products of the deodorized distillate or of the residue that remains after

removal of the esterified fatty acids from the product. After the solvent solution and the tocopherol-containing product have been allowed to stand, the upper layer (solvent layer) is separated and the solvent is removed from the upper layer obtained, leaving a tocopherol concentrate.

The ease of isolation of tocopherols from natural sources depends on the similarity of the properties of the impurities in relation to the solubility properties of the tocopherols. Dried sterols, for example, have properties similar to those of tocopherols and are extremely difficult to separate. Dried sterols have boiling points that lie so close to those of tocopherols that no known method of distillation is capable of separating them. Moreover, they can also not be removed in an effective manner by crystallization. Furthermore, they are not removed by aqueous basic extraction, since they are extracted into the organic phase together with the tocopherol.

It is a goal of the present invention to make available a process for the further purification of substances containing tocopherol by means of a series of two or more extractions, in order to exploit the differences in performance due to differences in extraction temperatures. Further goals ensue from the following description.

In accordance with the present invention, a series of two or more extractions at different extraction temperatures is carried out for each extraction. Such a process for the purification of tocopherol is comprised of:

(1) bringing a substance containing tocopherol into contact with an amount of methanol that is sufficient to form two phases, these phases consisting of
    (A) a methanol phase consisting of tocopherol and some impurities originally contained in the starting material and
    (B) a phase of impurities,
(2) separation of the phases,
(3) lowering of the temperature of the substance of phase (A) by an amount that is sufficient for a phase separation to take place and two phases to form, these phases consisting of

(C) a methanol phase enriched in tocopherol and

(D) a raffinate phase of tocopherol and impurities

(4) separation of the phases, and

(5) isolation of tocopherol from the substance of phase (C).

The substance of phases (B) and D) can be subjected to a further extraction. Furthermore, the substances of each of phases (B) and (D) can be employed as starting materials or can be combined with the starting material for the extraction of step 1 or 3.

The purification of tocopherol based on carrying out a series of extractions at different temperatures takes advantage of the differences existing for tocopherol solubility at different temperatures. The first extraction of step 1, performed at higher temperature, makes a larger amount of tocopherol soluble, since the solubility of tocopherol in methanol increases with temperature. The second extraction of step 3 at lower temperature is more selective and affords highly purified tocopherol.

If the temperature sequence is varied in such a way that the tocopherol is extracted first at lower temperature, then it would be possible to achieve the second extraction (of step 3) only with much difficulty. If a two-phase system were obtained, moreover, this would negatively affect the purity of the tocopherol. The purity is only optimized and improved in a multiple extraction process, in which different temperatures are employed for each extraction, by lowering the temperature on going from one extraction to the subsequent extraction.

For the present process, the methanol employed should be as dry as possible. The solubility of tocopherol decreases strongly when water is added to the methanol. For this reason, the methanol should preferably contain less than 1 wt % water.

The relevant volumes of methanol and starting material for which the extractions of step 1 and step 3 are carried out can also be adjusted and depend on such parameters as the tocopherol concentration in the starting material and the temperature chosen.

A lowering of the temperature of the material of the phase enriched in tocopherol brings about a further phase separation, so that a further extraction can be accomplished. Since the tocopherol in the methanol is better soluble at the lower temperatures than are the impurities at these temperatures, more purified tocopherol can be isolated from phase C than from phase D.

Preferred variants of the present invention can be employed. In one case, a preferred embodiment of the present invention requires, besides a lowering of the temperature of the separated methanol of phase A enriched in tocopherol, the addition of further starting material containing tocopherol during step 3 with further lowering of the temperature. In another preferred embodiment of the present invention, methanol is removed from the material of phase A after separation step 2 and before the second extraction at lower temperature of step 3.

After the separation of phases C and D, the tocopherol can be isolated by means of a suitable process, for example by crystallization, distillation, or stripping in vacuum or even by means of a further extraction. A less preferred method of isolation is the addition of water to the methanol phases enriched in tocopherol. Although the addition of water would cause the formation of a tocopherol phase that can be easily removed, the water can be removed from the methanol only with difficulty and a reuse of the methanol is hindered by the fact that the presence of water in the methanol impairs tocopherol extraction.

Preferably, the process is carried out in countercurrent, which makes it possible to bring about a number of phase contacts for each extraction. It is especially preferred to carry out these contacts stepwise, because the tocopherol that, originally, is distributed with the non-tocopherol impurities can be removed from the phase of the impurities during one of the later contacts, while, simultaneously, the impurities that were coextracted into the methanol can be removed and thereby enter the phase of the impurities.

Here, extraction refers to the dissolution and removal of a special component of a mixture into a solvent. Here, tocopherol is the component and methanol is the solvent. If a two-phase system can be prepared, then tocopherol can be extracted with methanol. If, in accordance with the

present invention, more than one extraction is carried out, whereby the temperature of the subsequent extraction is lower than that of the preceding extraction, the tocopherol finally separated in the methanol is of increasingly greater purity. Actually, the purity is optimized on account of the lowering of the temperature. Both tocopherol concentrates with various concentration values and natural organic sources can be used as starting materials for the present invention. Representative, but not exhaustive, examples of substances containing tocopherol are the following: safflower, soybeans, peanuts, cottonseed, linseed, sunflower seed, rapeseed, and palm oils. The starting substances can also be taken from other plant sources, such as, for example, palm leaves, lettuce, alfalfa, rubber, latex, and a diversity of other plant substances.

Included among substances that are typically found with tocopherol and can be separated as impurities are sterols, sterolic hydrocarbons, squalene, and hydrocarbons. These substances can, moreover, even be separated if they boil together with tocopherol.

The present invention can be applied in any respect to starting materials with low tocopherol content and equally to those with high tocopherol content. The temperature in the extraction of step 3 of the present invention is lowered by an amount that is sufficient to ensure a separation into two phases. The difference between the temperatures of the extraction of step 1 and the extraction of step 3 depends to a large extent on the circumstances and requirements of the individual case. For the extraction of step 3, the second tocopherol extraction, the temperature difference should be at least 15°C and preferably at least 20°C. This allows a temperature difference that is sufficient to ensure that the change in the solubility of the tocopherol and of the impurities results in the tocopherol of phase C being purer than the tocopherol of phase D. If desired, a phase separation could be ensured by the removal of methanol or, alternatively, an organic material containing tocopherol can be added as starting material for the second extraction.

Preferably, the temperature of each extraction is adjusted to the tocopherol concentration in the starting material. This makes possible the advantageous exploitation of the solubility differences of tocopherol at different temperatures. If, for example, tocopherol is extracted with methanol at

low temperatures, less tocopherol goes into solution, but the tocopherol has a very much greater purity than it would exhibit at higher temperatures. For this reason, an extraction at low temperature is performed with advantage if a starting material has a low tocopherol content, since, then, the tocopherol is extracted more selectively and thus with less impurities. The tocopherol concentrate obtained is of very much higher purity.

Any desired organic material containing tocopherol can be employed for this process. Suitable starting materials can contain 3 to 35 wt %, 35 to 50 wt %, or 50 to 75 wt % and even 75 to 95 wt % tocopherol. If the starting material contains tocopherol in an amount of more than 75 wt %, it is preferred that the second extraction be carried out at a temperature below 25°C.

Although the exact difference between the temperatures of the extraction of step 1 and the extraction of step 3 depend strongly on the circumstances and requirements of the individual case, the temperature difference should be at least 15°C and preferably at least 20°C. In each case, the exact temperatures of the two extractions of step 1 and step 3 can be set at any two points within the range in which methanol is liquid. In practical terms, however, the extraction at the low temperature (of step 3) should be carried out at or below ambient temperature (25°C) and, in such a case, the extraction at the high temperature would be carried out at least 15°C and preferably at least 20°C higher. Thus, the extraction at the low temperature could be carried out advantageously at a temperature in the range of about 25°C to about 60°C, whereby the higher temperature is elevated to any point from about 40°C to about 100°C. In a further sense, the extraction can be carried out in a suitable way at a low temperature in the range of about -98°C to about 60°C, while the extraction at the high temperature (of step 1) would be carried out in a suitable way in the range of about 10°C to about 100°C. Preferably, the extraction at the low temperature is carried out at a temperature in the range of about -10°C to about 60°C, while the extraction at the high temperature is carried out in the range of about 40°C to about 90°C.

An extraction at the high temperature can make possible, to advantage, a higher solubility of the tocopherol in the methanol phase. At pressures above atmospheric pressure, still higher temperatures can even be employed. The pressure employed in the present process can be

approximately 1 to 4 bar (1 to 4 atmospheres). At 4 bar (4 atmospheres) the maximum temperature presumably lies at approximately 100°C. For temperatures up to 90°C, the preferred pressure range is about 1 to about 3 bar (about 1 to about 3 atmospheres). Naturally, the minimum temperature permitted for the extraction at the low temperature is the freezing point of methanol.

If the extraction of step 3 is carried out, the tocopherol can be isolated by gradually lowering the temperature, whereby the gradual formation of the separate phases is brought about. This makes possible either the gradual removal of the phases being formed or their periodic removal or isolation at various stages in the formation of the tocopherol phase. Here, it is important to ascertain that the phase being formed tends to exhibit a higher ratio of impurities to tocopherol than does the methanol phase (C) from which it forms. Consequently, the newly formed phase (phase D) is not as pure with respect to tocopherol as the material isolated from phase C after the removal of methanol. If, in the gradual or periodic removal of the phase being formed, the temperature is not lowered to the freezing point of methanol, then the methanol remaining after removal of the tocopherol phase should be removed by distillation in order to obtain the purest tocopherol.

Another important variable that can be used is the volume. The respective volumes of the starting material and the methanol can be adjusted to each other throughout a diversity of temperatures in such a way that the presence of a two-phase system is always ensured. The extraction at the low temperature can be carried out with a larger volume of methanol relative to the volume of the starting material in order to maximize the tocopherol yield. Accordingly, the volume ratios of methanol to starting material can vary from about 1.5 : 1 to about 20 : 1 and preferably from about 2 : 1 to about 12 : 1. Presumably, the volume ratio of methanol to starting material for the extraction at high temperature can be about 1 : 1 to about 12 : 1.

A large number of different isolation methods can be employed for separation of the tocopherol from the substance of the methanol phase. These methods include crystallization, vacuum distillation, precipitation, adsorption, or even the addition of water or another polar substance

that brings about the formation of a separate tocopherol phase. Independent of which step of isolation is employed, the temperatures and pressures used should be appropriate to the special type of isolation employed.

After the extractions of step 1 or step 3, the impurities in the phase material of phase D and often also of phase B contain certain amounts of tocopherol. In such a case, a further extraction can be performed in order to isolate this tocopherol or else the substance can be combined with additional starting material. More preferred, however, is the use of a system for the continuous, stepwise extraction in such a way that a number of phase contacts are brought about. Such a system used for the overall process (both the extraction of step 1 and the extraction of step 3) reduces to a minimum the amount of tocopherol disposed of , together with the impurities, as waste and also reduces the amount of impurities that remain in the methanol enriched in tocopherol.

Any apparatus suitable for liquid / liquid phase extractions can be used. Consequently, the process can be carried out batchwise or continuously. Preferably, however, a continuously operating extraction system is utilized. The very especially preferred continuous process provides for a number of countercurrent phase contacts (a continuous, multistage countercurrent system). If these contacts occur stagewise, tocopherol that has remained originally in the impurity-containing organic material is transferred to the methanol in a subsequent stage. In the same way, impurities that originally ended up in the methanol during the distribution are transferred to the nonpolar phase during the subsequent phase contacts. Such a system produces, in accordance with the present invention, tocopherol both in high yield and with high purity.

The process in accordance with the present invention is illustrated in detail by the following examples. These examples are intended for clarification and demonstration of the present invention, but not as limitations thereof. Unless otherwise stated, all parts and percents refer to the weight.

Example I

For the first step, two extractions were carried out at room temperature (about 24°C). The starting material utilized contained 64.5 wt % tocopherol. In extraction one of the first step, 100 g of starting material was mixed with 400 g of methanol; in extraction two of the first step, 83 g of starting material was mixed with 325 g of methanol. In each extraction, phases A and B formed:

Phase A - methanol phase that contained tocopherol and some impurities originally present in the starting material;

Phase B - phase of the impurities (raffinate).

Phases A and B were separated and the phases A of the two extractions were combined; then, a sufficient amount of methanol was removed therefrom so that the solids concentration in the combined phase increased from 12.6 wt % to 20 wt %. Afterwards, the temperature of the remaining combined phase was reduced to 4°C (reduction to about 20°C), whereby a new two-phase system formed from:

Phase C - a methanol phase enriched in tocopherol; and

Phase D - a raffinate phase consisting of tocopherol and impurities.

Samples of all six phases were analyzed (see Tables 1 and 2).

Table 1 (at 24°C)

Extraction	Phase	Total weight of the phase g	Total weight of the solids g	Tocopherol proportion in the solids wt %	Total weight of the tocopherol g
1	A	432	54.3	75.5	41.0
	B	64.1	46	50.7	23.3
2	A	355.6	44.7	75.5	33.7
	B	52.8	37.9	50.7	19.2

Table 2 (at 4°C)

Phase	Total weight of the phase g	Total weight of the solids g	Tocopherol proportion in the solids wt %	Total weight of the tocopherol
C	427.1	66	78.3	51.7
D	70.8	33	66.8	22.0

Example II

Two extractions were carried out by using two columns connected in series. Column 1 was maintained at 50°C. Pure methanol was fed into its lower end and passed in countercurrent in such a way that it came into contact with the starting material, which contained 39.4 wt % tocopherol and was applied to the head of the column. The starting material used for column 1 was the raffinate from the extraction carried out in column 2.

After the extraction in column 1 at 50°C, the methanol enriched in tocopherol was fed into column 2, which was maintained at 20°C; additional starting material containing 48.3 wt % tocopherol was passed in countercurrent in such a way that it came into contact with the methanol containing tocopherol. The raffinate from column 2 was then used as starting material for column 1. Samples were taken in each case from the methanol enriched in tocopherol both after column 1 and after column 2. In addition, samples of the starting materials for columns 1 and 2 and from the raffinate remaining after column 2 were taken. The analysis results are listed below.

Table 3

Analysis results after removal of the methanol from the samples

Sample	Tocopherol proportion in the solids wt %	Proportion of low-boiling impurities in the solids wt %
Methanol phase enriched in tocopherol after column 1	48.1	10.8
Methanol phase enriched in tocopherol after column 2	74.0	2.2
Starting material for column 2	48.3	5.6
Raffinate from column 2, used as starting material for column 1	39.4	10.3
Final raffinate from column 1	19.1	13.7

After the second extraction at 20°C, about 81% of the total amount of the tocopherol (originally present in the starting material) was present in the methanol phase and about 19% of the tocopherol had remained in the final raffinate of the starting material.